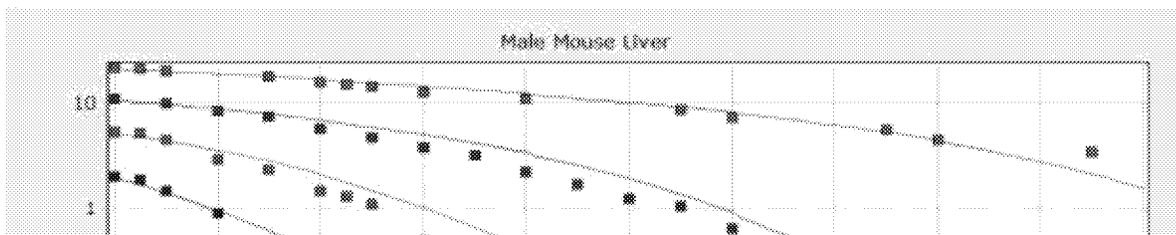
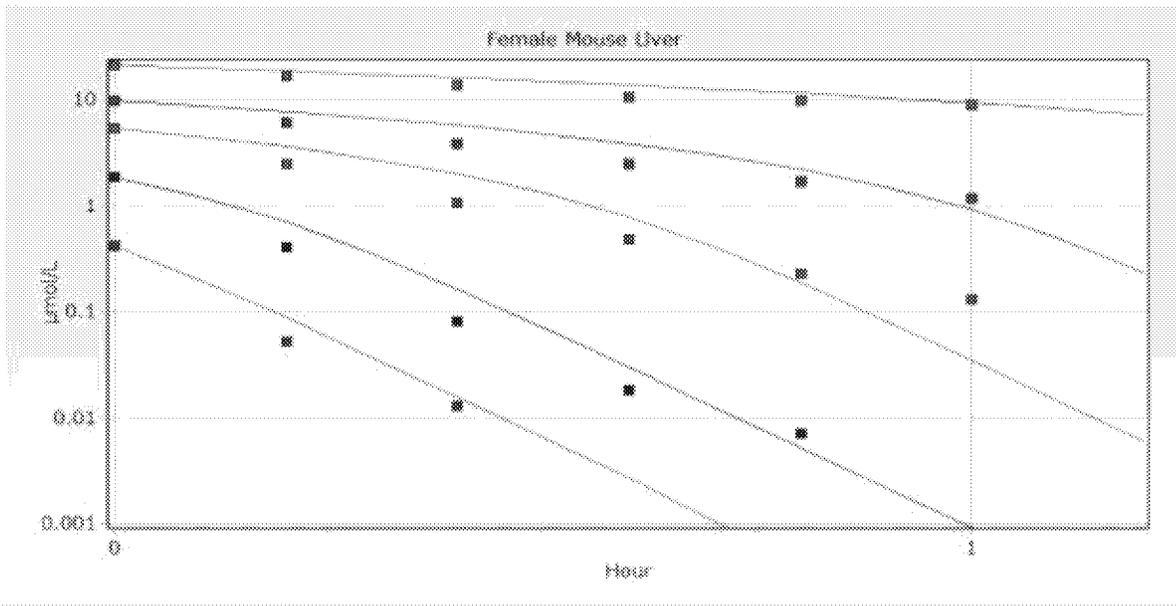


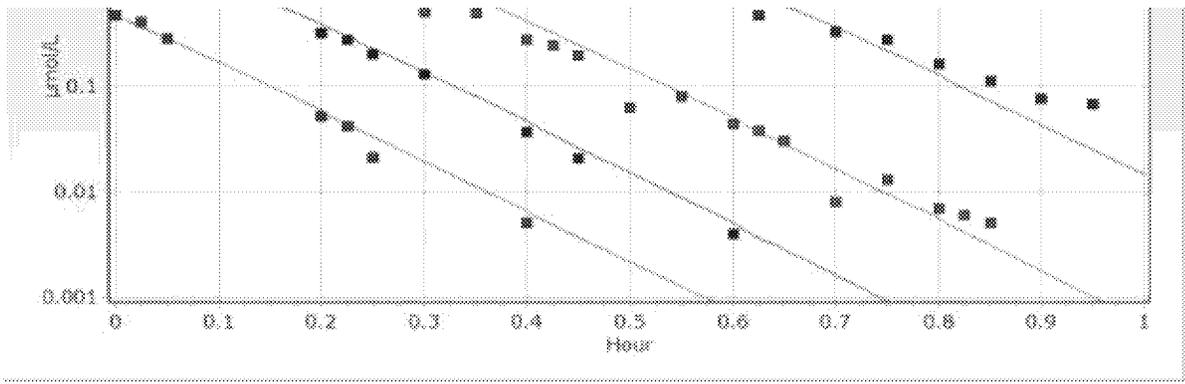
		Female			
		Average		95% CI	
Log	Vmax	$\mu\text{mol/hr/mg protein}$	-2.22	-2.41	-2.03
	Km	$\mu\text{mol/L}$	-0.77	-1.17	-0.38

		Male			
		Average		95% CI	
	Vmax	$\mu\text{mol/hr/mg protein}$	-1.47	-1.53	-1.41
	Km	$\mu\text{mol/L}$	-0.49	-0.62	-0.37

		Female			
		Average		95% CI	
EXP	Vmax	$\mu\text{mol/hr/mg protein}$	0.108	0.090	0.13
	Km	$\mu\text{mol/L}$	0.46	0.31	0.69

		Male			
		Average		95% CI	
	Vmax	$\mu\text{mol/hr/mg protein}$	0.230	0.22	0.24
	Km	$\mu\text{mol/L}$	0.612	0.54	0.69





```
gelman.diag(x, autoburnin=FALSE)
```

```
Potential scale reduction factors:
```

	Point	est.	Upper	C.I.
LI		1	1	
Vmax		1	1	
Km		1	1	

```
Multivariate psrf
```

```
1
```

```
>
```

```
> summary(x1)
```

```
Iterations = 1:10000
Thinning interval = 1
Number of chains = 1
Sample size per chain = 10000
```

```
1 Empirical plus mean and standard error of the standard deviation for each variable, plus the mean:
```

	Mean	SD	Naive SE	Time-series SE
LI	0.4676	0.07259	0.0007259	0.001322
Vmax	-2.2249	0.09873	0.0009873	0.005343
Km	-0.7689	0.20406	0.0020406	0.010945

```
2 Quantiles for each variable:
```

	2.50%	25%	50%	75%	97.50%
LI	0.3498	0.4162	0.4581	0.5098	0.6349
Vmax	-2.4128	-2.2913	-2.2245	-2.1606	-2.0291
Km	-1.1709	-0.9033	-0.7703	-0.6328	-0.3762

```
> summary(x2)
```

```
Iterations = 1:10000
Thinning interval = 1
Number of chains = 1
Sample size per chain = 10000
```

```
1 Empirical plus mean and standard error of the standard deviation for each variable, plus the mean:
```

```
Mean SD Naive SE Time-series SE
```

```

LI          0.4657  0.07228  0.0007228  0.001437
Vmax       -2.227  0.09753  0.0009753  0.005162
Km         -0.7733  0.20047  0.0020047  0.010622

```

2 Quantiles for each variable:

```

          2.50%   25%   50%   75%   97.50%
LI        0.3515  0.4148  0.4565  0.5075  0.6288
Vmax     -2.4147 -2.2905 -2.2276 -2.1648 -2.0289
Km       -1.166  -0.9031 -0.7744 -0.6474 -0.3813

```

> summary(x3)

```

Iterations = 1:10000
Thinning interval = 1
Number of chains = 1
Sample size per chain = 10000

```

1 Empirical plus mean and standard error of the standard deviation for each variable, the mean:

```

          Mean          SD      Naive      SE      Time-series SE
LI          0.4668  0.07275  0.0007275  0.001521
Vmax       -2.221  0.09732  0.0009732  0.005156
Km        -0.7599  0.19733  0.0019733  0.010606

```

2 Quantiles for each variable:

```

          2.50%   25%   50%   75%   97.50%
LI        0.351  0.4156  0.458  0.5072  0.6381
Vmax     -2.412 -2.2834 -2.2215 -2.157  -2.0344
Km       -1.151 -0.8899 -0.7583 -0.628  -0.3843

```

gelman.diag(x, autoburnin=FALSE)

Potential scale reduction factors:

	Point	est.	Upper	C.I.
LI		1	1	
Vmax		1	1	
Km		1	1	

Multivariate psrf

1

>

> summary(x1)

Iterations = 1:10000
 Thinning interval = 1
 Number of chains = 1
 Sample size per chain = 10000

1 Empirical plus mean and standard error of standard deviation for each variable, the mean:

	Mean	SD	Naive	SE	Time-series SE
LI	0.3093	0.02639	0.0002639	0.000432	
Vmax	-1.4697	0.0292	0.000292	0.00148	
Km	-0.4912	0.06384	0.0006384	0.003181	

2 Quantiles for each variable:

	2.50%	25%	50%	75%	97.50%
LI	0.2623	0.2911	0.3076	0.3263	0.3645
Vmax	-1.5259	-1.4889	-1.4695	-1.4495	-1.4137
Km	-0.6175	-0.5338	-0.4903	-0.4478	-0.3681

> summary(x2)

Iterations = 1:10000
 Thinning interval = 1
 Number of chains = 1
 Sample size per chain = 10000

1 Empirical plus mean and standard error of standard deviation for each variable, the mean:

Mean SD Naive SE Time-series SE

LI	0.3089	0.02592	0.0002592	0.000423
Vmax	-1.4696	0.0313	0.000313	0.001734
Km	-0.4911	0.06778	0.0006778	0.003782

2 Quantiles for each variable:

	2.50%	25%	50%	75%	97.50%
LI	0.2648	0.2902	0.3073	0.3248	0.3647
Vmax	-1.5289	-1.4901	-1.4712	-1.4491	-1.4054
Km	-0.6202	-0.535	-0.4942	-0.4463	-0.3491

> summary(x3)

Iterations	=	1:10000			
Thinning	interval	=	1		
Number	of	chains	=	1	
Sample	size	per	chain	=	10000

1 Empirical plus mean and standard error of the standard deviation for each variable, the mean:

	Mean	SD	Naive	SE	Time-series SE
LI	0.3088	0.02604	0.0002604	0.000427	
Vmax	-1.4675	0.02963	0.0002963	0.001581	
Km	-0.487	0.06418	0.0006418	0.003413	

2 Quantiles for each variable:

	2.50%	25%	50%	75%	97.50%
LI	0.2637	0.29	0.3076	0.3253	0.3639
Vmax	-1.5278	-1.487	-1.4681	-1.4477	-1.4101
Km	-0.6179	-0.527	-0.4878	-0.4446	-0.3608

Female

Female

Log			Average	95% CI	
	Vmax	$\mu\text{mol/hr/mg protein}$	-3.58	-3.91	-3.25
Km	$\mu\text{mol/L}$	1.07	0.69	1.44	

Male

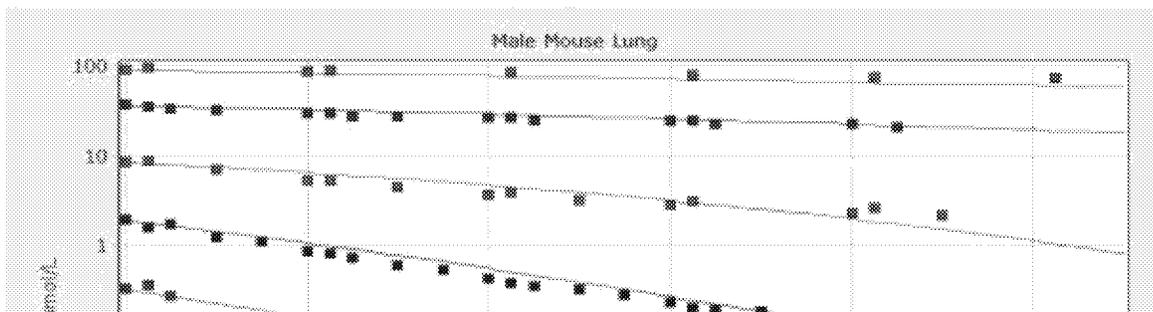
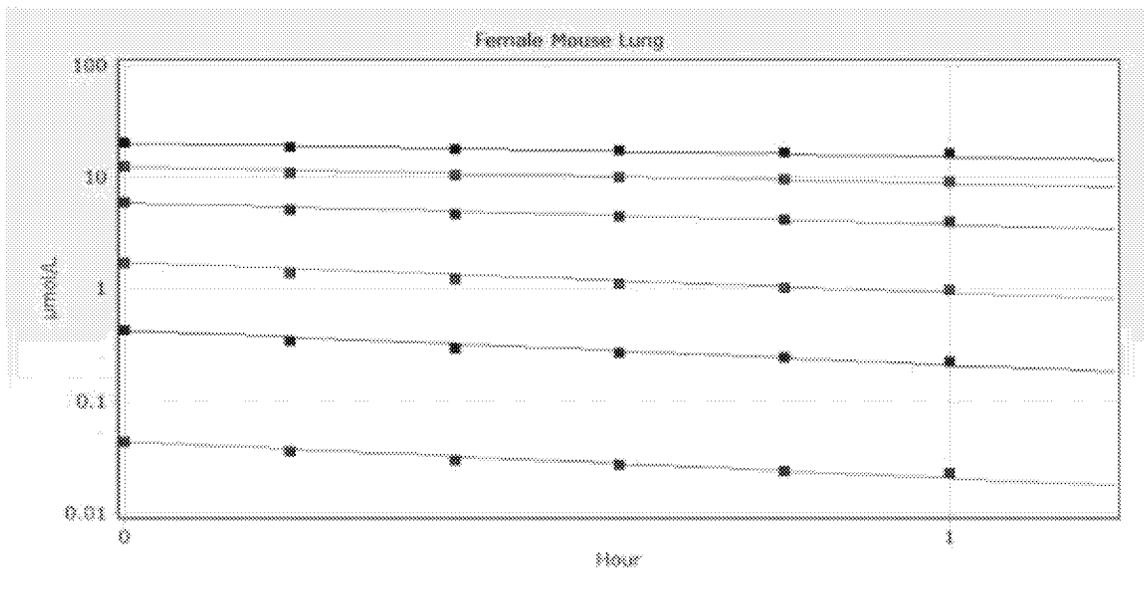
		Average	95% CI	
Vmax	$\mu\text{mol/hr/mg protein}$	-2.03	-2.14	-1.90
Km	$\mu\text{mol/L}$	0.54	0.41	0.70

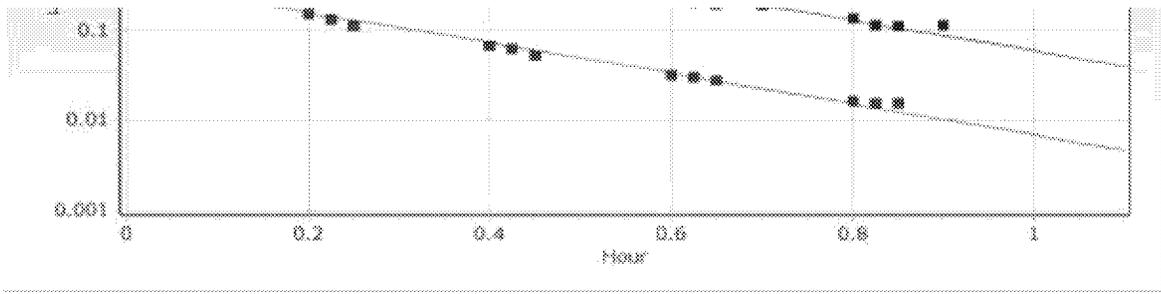
Female

EXP			Average	95% CI	
	Vmax	$\mu\text{mol/hr/mg protein}$	0.028	0.020	0.039
Km	$\mu\text{mol/L}$	2.91	1.99	4.24	

Male

		Average	95% CI	
Vmax	$\mu\text{mol/hr/mg protein}$	0.13	0.12	0.15
Km	$\mu\text{mol/L}$	1.72	1.51	2.02





gelman.diag(x, autoburnin=FALSE)

Potential scale reduction factors:

	Point	est.	Upper	C.I.
LI		1	1	
Vmax		1.02	1.06	
Km		1.02	1.06	

Multivariate psrf

1.02

>

> summary(x1)

Iterations = 1:10000
 Thinning interval = 1
 Number of chains = 1
 Sample size per chain = 10000

1 Empirical plus mean and standard deviation for each variable, standard error of the mean:

	Mean	SD	Naive	SE	Time-series SE
LI	0.05712	0.007288	7.29E-05	1.26E-04	
Vmax	-3.57856	0.167052	1.67E-03	1.50E-02	
Km	1.06718	0.192112	1.92E-03	1.75E-02	

2 Quantiles for each variable:

	2.50%	25%	50%	75%	97.50%
LI	0.04514	0.05201	0.0564	6.13E-02	7.34E-02
Vmax	-3.90942	-3.69267	-3.5756	-3.46475	-3.25309
Km	0.68801	0.93497	1.0704	1.20E+00	1.44E+00

> summary(x2)

Iterations = 1:10000
 Thinning interval = 1
 Number of chains = 1
 Sample size per chain = 10000

1 Empirical plus mean and standard deviation for each variable, standard error of the mean:

	Mean	SD	Naive	SE	Time-series SE
LI	0.05717	0.007458	7.46E-05	1.32E-04	
Vmax	-3.62744	0.153111	1.53E-03	1.22E-02	

Km 1.01099 0.176328 1.76E-03 1.39E-02

2 Quantiles for each variable:

	2.50%	25%	50%	75%	97.50%
LI	0.04506	0.05192	0.05639	0.06148	0.07407
Vmax	-3.91588	-3.72782	-3.6303	-3.53244	-3.30676
Km	0.68354	0.8949	1.0068	1.12108	1.38889

> summary(x3)

Iterations = 1:10000
 Thinning interval = 1
 Number of chains = 1
 Sample size per chain = 10000

1 Empirical plus mean and standard deviation for each variable, standard error of the mean:

	Mean	SD	Naive SE	Time-series SE
LI	0.05725	0.007307	7.31E-05	1.42E-04
Vmax	-3.58837	0.171506	1.72E-03	1.50E-02
Km	1.05708	0.197345	1.97E-03	1.74E-02

2 Quantiles for each variable:

	2.50%	25%	50%	75%	97.50%
LI	0.04502	0.05204	5.66E-02	0.06164	0.07368
Vmax	-3.94569	-3.70485	-3.58E+00	-346.42%	-328%
Km	0.64471	0.92227	1.06243	1.19907	1.42067

Male gelman.diag(x, autoburnin=FALSE)

Potential scale reduction factors:

	Point	est.	Upper	C.I.
LI		1	1	
Vmax		1.01	1.03	
Km		1.01	1.03	

Multivariate psrf

1.01

>

> summary(x1)

Iterations = 1:10000
Thinning interval = 1
Number of chains = 1
Sample size per chain = 10000
1 Empirical mean and standard deviation for each variable, plus standard error of the mean:

	Mean	SD	Naive	SE	Time-series SE
LI	0.15	1.26E-02	1.26E-04	0.0002108	
Vmax	-2.0324	5.98E-02	5.98E-04	0.0054991	
Km	0.5426	0.07296	0.0007296	0.0066262	

2 Quantiles for each variable:

	2.50%	25%	50%	75%	97.50%
LI	0.1283	1.41E-01	1.49E-01	0.1579	0.1777
Vmax	-2.1416	-2.0738	-2.0341	-1.9979	-1.8976
Km	0.4094	4.93E-01	5.41E-01	0.5853	0.7042

> summary(x2)

Iterations = 1:10000
Thinning interval = 1
Number of chains = 1
Sample size per chain = 10000
1 Empirical mean and standard deviation for each variable, plus standard error of the mean:

	Mean	SD	Naive	SE	Time-series SE
LI	0.1501	0.01273	0.0001273	0.0002192	
Vmax	-2.0425	0.05586	0.0005586	0.004609	

Km 0.5302 0.06889 0.0006889 0.0056812

2 Quantiles for each variable:

	2.50%	25%	50%	75%	97.50%
LI	0.1273	0.141	0.1491	0.1582	0.1773
Vmax	-2.1532	-2.0774	-2.0426	-2.0102	-1.9203
Km	0.3939	0.4869	0.5294	0.5702	0.6768

> summary(x3)

Iterations = 1:10000
Thinning interval = 1
Number of chains = 1
Sample size per chain = 10000

1 Empirical mean and standard deviation for each variable, plus standard error of the mean:

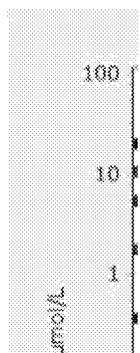
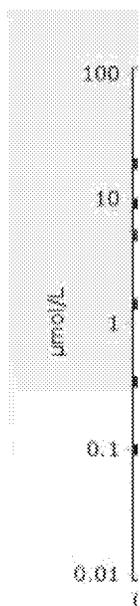
	Mean	SD	Naive SE	Time-series SE
LI	0.1504	0.01272	0.0001272	0.0002134
Vmax	-2.0315	0.05622	0.0005622	0.0045976
Km	0.5444	0.06879	0.0006879	0.0057819

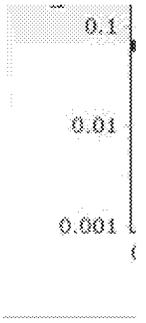
2 Quantiles for each variable:

	2.50%	25%	50%	75%	97.50%
LI	0.1278	0.1414	0.1497	0.1585	0.1775
Vmax	-2.1342	-2.0695	-2.0338	-1.9979	-1.9093
Km	0.4199	0.4984	0.5421	0.5851	0.6904

Log

EXP





Female

KF

Male

Vmax

Km

Female

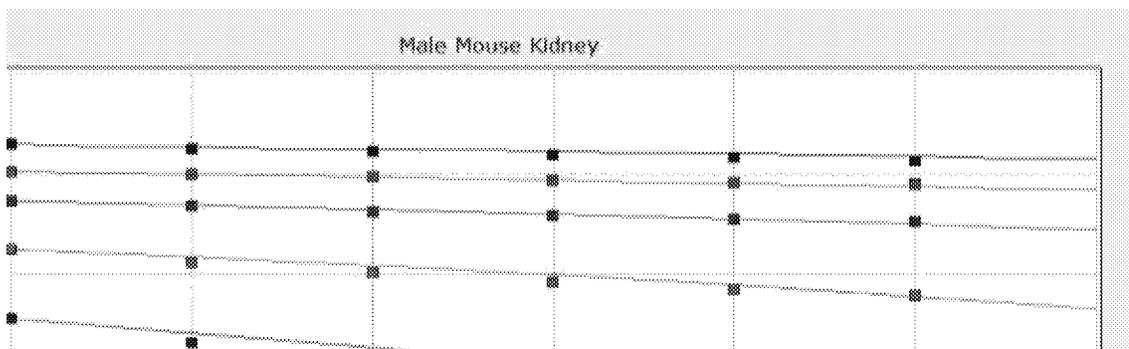
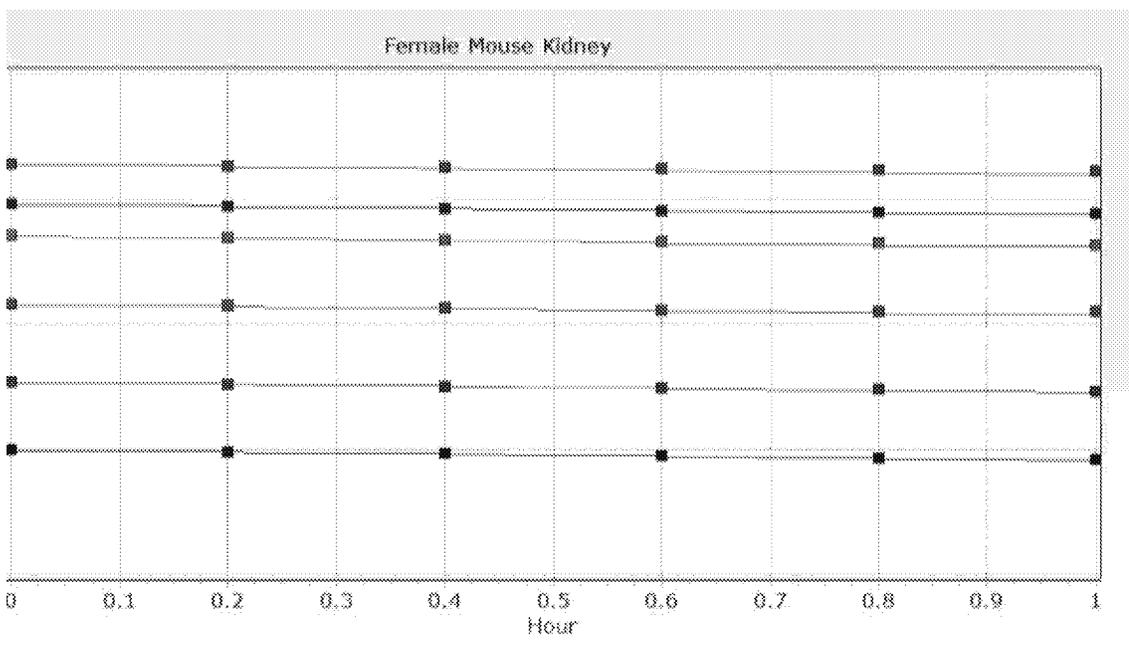
KF

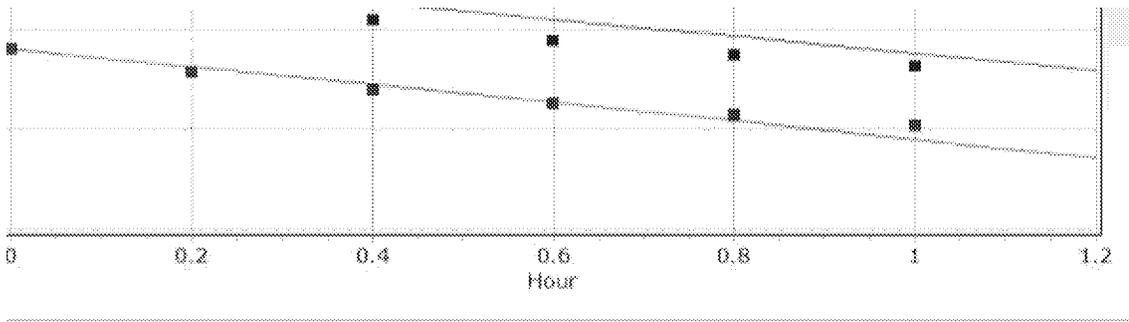
Note: 2 mg of protein used in assay (VK was not scaled in the in vitro model - lung was 1 mg so not needed)

Male

Vmax

Km





Female

	Average	95% CI	
L/hr/mg protein	-7.056	-7.896	-6.553

	Average	95% CI	
μmol/hr/mg protein	-4.59	-4.86	-4.32
μmol/L	-0.55	-0.87	-0.23

	Average	95% CI	
L/hr/mg protein	0.00043	0.00019	0.00071

	Average	95% CI	
μmol/hr/mg protein	0.010	0.008	0.013
μmol/L	0.58	0.42	0.79

gelman.diag(x, autoburnin=FALSE)

Male

Potential scale reduction factors:

	Point	est.	Upper	C.I.
LI		1	1	
KF		1	1	

Multivariate psrf

1

>

> summary(x1)

Iterations = 1:10000
 Thinning interval = 1
 Number of chains = 1
 Sample size per chain = 10000

1 Empirical plus mean and standard deviation for each variable, standard error of the mean:

	Mean	SD	Naive	SE	Time-series SE
LI	0.05436	0.006977	6.98E-05	0.0001247	
KF	-7.0563	0.347454	3.48E-03	0.0066822	

2 Quantiles for each variable:

	2.50%	25%	50%	75%	97.50%
LI	0.04267	0.04948	0.05357	0.05872	0.06954
KF	-7.90	-7.22	-7.00	-6.82	-6.55

> summary(x2)

Iterations = 1:10000
 Thinning interval = 1
 Number of chains = 1
 Sample size per chain = 10000

1 Empirical plus mean and standard deviation for each variable, standard error of the mean:

	Mean	SD	Naive	SE	Time-series SE
LI	0.05426	0.006831	6.83E-05	0.0001224	
KF	-7.06236	0.352842	3.53E-03	0.0073882	

2 Quantiles for each variable:

	2.50%	25%	50%	75%	97.50%
LI	0.04286	0.04942	0.05366	0.05831	0.0696
KF	-7.91035	-7.22355	-7.00181	-6.83392	-6.5666

> summary(x3)

Iterations = 1:10000
 Thinning interval = 1
 Number of chains = 1
 Sample size per chain = 10000

1 Empirical mean and standard deviation for each variable, plus standard error of the mean:

	Mean	SD	Naive SE	Time-series SE
LI	0.05438	0.006972	6.97E-05	0.0001352
KF	-7.07084	0.354618	3.55E-03	0.0070147

2 Quantiles for each variable:

	2.50%	25%	50%	75%	97.50%
LI	0.04282	0.04945	0.05362	0.05847	0.06985
KF	-7.91999	-7.22633	-7.01231	-6.84524	-6.55977

gelman.diag(x, autoburnin=FALSE)

Potential scale reduction factors:

	Point	est.	Upper	C.I.
LI		1	1	
Vmax		1	1	
Km		1	1	

Multivariate psrf

1

>

> summary(x1)

Iterations = 1:10000
 Thinning interval = 1
 Number of chains = 1
 Sample size per chain = 10000

1 Empirical plus mean and standard error of standard deviation for each variable, the mean:

	Mean	SD	Naive	SE	Time-series SE
LI	0.1668	2.14E-02	2.14E-04	0.0003892	
Vmax	-4.5935	1.38E-01	1.38E-03	0.0101186	
Km	-0.552	0.163	0.00163	0.0119514	

2 Quantiles for each variable:

	2.50%	25%	50%	75%	97.50%
LI	0.1312	1.52E-01	1.65E-01	0.1798	0.214
Vmax	-4.8606	-4.6882	-4.5891	-4.5057	-4.315
Km	-0.8682	-6.63E-01	-5.52E-01	-0.4457	-0.231

> summary(x2)

Iterations = 1:10000
 Thinning interval = 1
 Number of chains = 1
 Sample size per chain = 10000

1 Empirical plus mean and standard error of standard deviation for each variable, the mean:

	Mean	SD	Naive	SE	Time-series SE
LI	0.1668	0.02106	0.0002106	0.0003764	
Vmax	-4.6043	0.14446	0.0014446	0.0103371	

Km -0.563 0.1714 0.001714 0.0124802

2 Quantiles for each variable:

	2.50%	25%	50%	75%	97.50%
LI	0.1317	0.1519	0.1649	0.1791	0.2151
Vmax	-4.8867	-4.7005	-4.6021	-4.5126	-4.3084
Km	-0.9081	-0.6784	-0.5623	-0.4552	-0.2094

> summary(x3)

Iterations = 1:10000
 Thinning interval = 1
 Number of chains = 1
 Sample size per chain = 10000

1 Empirical plus mean and standard deviation for each variable, standard error of the mean:

	Mean	SD	Naive SE	Time-series SE
LI	0.1671	0.02115	0.0002115	0.0003597
Vmax	-4.5944	0.14189	0.0014189	0.0099935
Km	-0.5529	0.16812	0.0016812	0.0116754

2 Quantiles for each variable:

	2.50%	25%	50%	75%	97.50%
LI	0.1322	0.1523	0.1652	0.1801	0.214
Vmax	-4.8713	-4.6878	-4.593	-4.5042	-4.3089
Km	-0.8801	-0.6603	-0.5517	-0.4467	-0.2155

Female

Female

			Average	95% CI	
Log	Vmax	$\mu\text{mol/hr/mg protein}$	-2.64	-2.85	-2.44
	Km	$\mu\text{mol/L}$	-0.30	-0.57	-0.04

Male

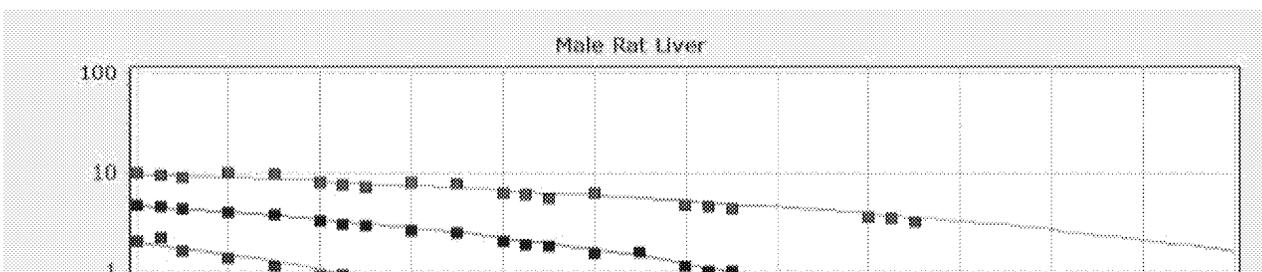
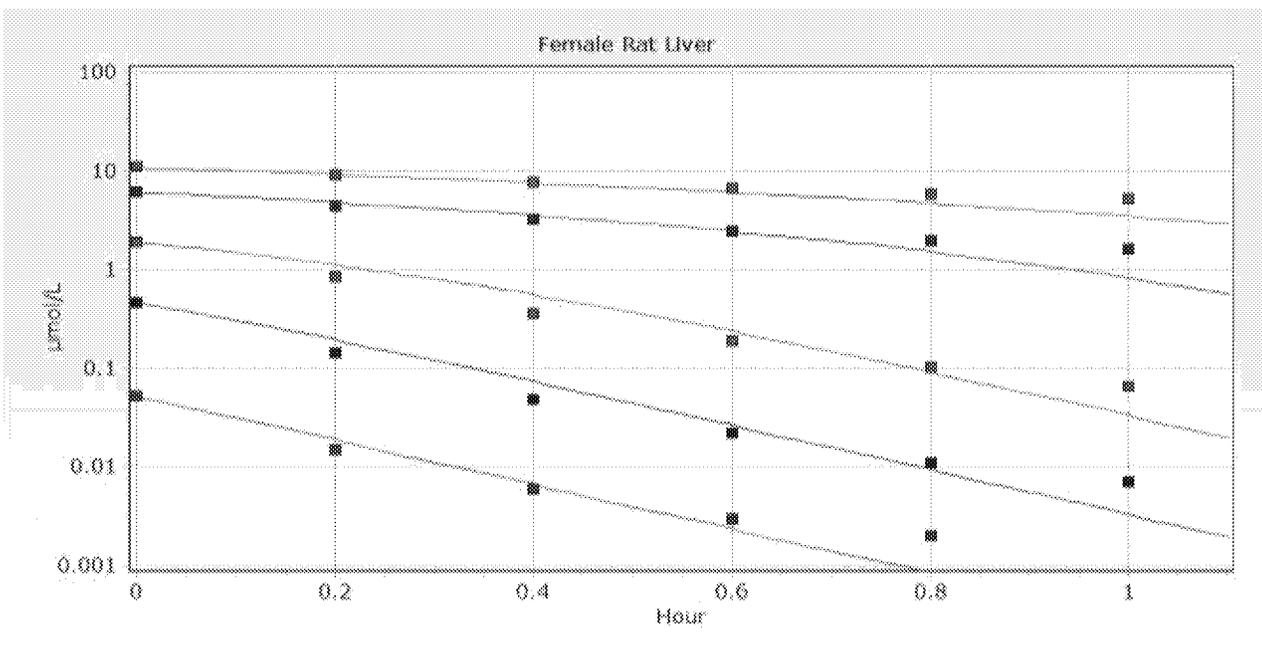
			Average	95% CI	
	Vmax	$\mu\text{mol/hr/mg protein}$	-2.65	-2.69	-2.61
	Km	$\mu\text{mol/L}$	-1.06	-1.15	-0.97

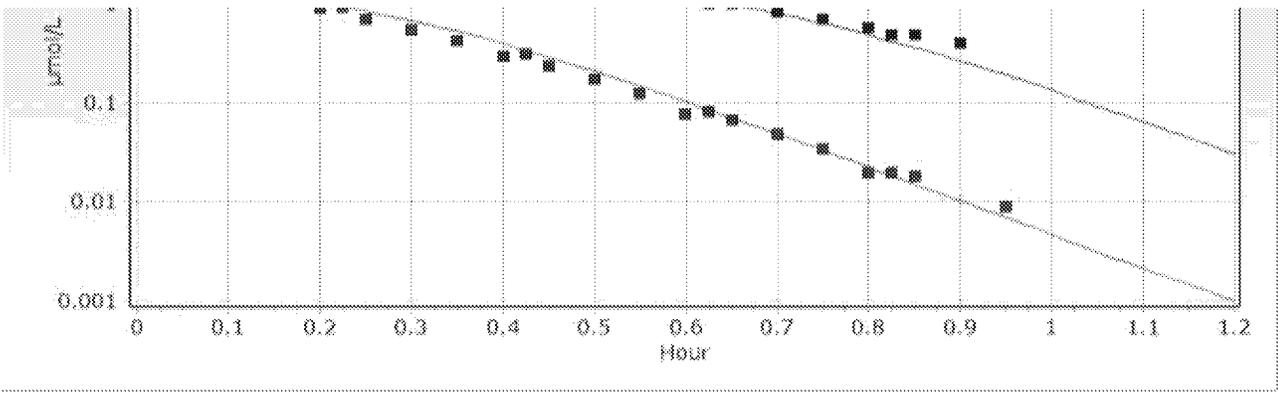
Female

			Average	95% CI	
EXP	Vmax	$\mu\text{mol/hr/mg protein}$	0.072	0.058	0.087
	Km	$\mu\text{mol/L}$	0.74	0.57	0.96

Male

			Average	95% CI	
	Vmax	$\mu\text{mol/hr/mg protein}$	0.071	0.068	0.074
	Km	$\mu\text{mol/L}$	0.35	0.32	0.38





gelman.diag(x, autoburnin=FALSE)

Male

Potential scale reduction factors:

	Point	est.	Upper	C.I.
LI		1	1	
Vmax		1	1	
Km		1	1	

Multivariate psrf

1

>

> summary(x1)

Iterations = 1:10000
 Thinning interval = 1
 Number of chains = 1
 Sample size per chain = 10000

1 Empirical plus mean and standard error of standard deviation for each variable, the mean:

	Mean	SD	Naive	SE	Time-series SE
LI	0.3036	0.04508	0.0004508	0.0008033	
Vmax	-2.6364	0.10084	0.0010084	0.0069003	
Km	-0.2997	0.12941	0.0012941	0.0086726	

2 Quantiles for each variable:

	2.50%	25%	50%	75%	97.50%
LI	0.2305	0.2716	0.2979	0.3311	0.4064
Vmax	-284.82%	-270%	-264%	-257%	-244.19%
Km	-0.5655	-0.3801	-0.2997	-0.2163	-0.04314

> summary(x2)

Iterations = 1:10000
 Thinning interval = 1
 Number of chains = 1
 Sample size per chain = 10000

1 Empirical plus mean and standard error of standard deviation for each variable, the mean:

	Mean	SD	Naive	SE	Time-series SE
LI	0.3036	0.04408	0.0004408	0.0007371	
Vmax	-2.6348	0.10162	0.0010162	0.0067663	

Km -0.2994 0.13007 0.0013007 0.008482

2 Quantiles for each variable:

	2.50%	25%	50%	75%	97.50%
LI	0.2321	0.2713	0.2983	0.3293	0.40211
Vmax	-2.8249	-2.7046	-2.637	-2.5725	-2.42029
Km	-0.5443	-0.3869	-0.3033	-0.2192	-0.01368

> summary(x3)

Iterations = 1:10000
Thinning interval = 1
Number of chains = 1
Sample size per chain = 10000

1 Empirical mean and standard deviation for each variable,
plus standard error of the mean:

	Mean	SD	Naive SE	Time-series SE
LI	0.3042	0.04407	0.0004407	0.0008181
Vmax	-2.6326	0.09537	0.0009537	0.0057904
Km	-0.2953	0.12156	0.0012156	0.0075017

2 Quantiles for each variable:

	2.50%	25%	50%	75%	97.50%
LI	0.2329	0.272	0.2989	0.3305	0.40475
Vmax	-2.8233	-2.697	-2.6305	-2.567	-2.4509
Km	-0.5337	-0.38	-0.2928	-0.2123	-0.06394

gelman.diag(x, autoburnin=FALSE)

Potential scale reduction factors:

	Point	est.	Upper	C.I.
LI		1	1	
Vmax		1	1	
Km		1	1	

Multivariate psrf

1

>

> summary(x1)

Iterations = 1:10000
 Thinning interval = 1
 Number of chains = 1
 Sample size per chain = 10000

1 Empirical plus mean and standard error of standard deviation for each variable, the mean:

	Mean	SD	Naive	SE	Time-series SE
LI	0.1343	0.01211	0.0001211	0.0002019	
Vmax	-2.6517	0.02121	0.0002121	0.0013015	
Km	-1.0562	0.04554	0.0004554	0.0028226	

2 Quantiles for each variable:

	2.50%	25%	50%	75%	97.50%
LI	0.1132	0.1255	0.1335	0.1421	0.1604
Vmax	-269.32%	-267%	-265%	-264%	-260.93%
Km	-1.1479	-1.086	-1.0565	-1.0264	-0.966

> summary(x2)

Iterations = 1:10000
 Thinning interval = 1
 Number of chains = 1
 Sample size per chain = 10000

1 Empirical plus mean and standard error of standard deviation for each variable, the mean:

	Mean	SD	Naive	SE	Time-series SE
LI	0.134	0.01204	0.0001204	0.0002054	
Vmax	-2.652	0.02063	0.0002063	0.0012104	

Km -1.056 0.04378 0.0004378 0.002598

2 Quantiles for each variable:

	2.50%	25%	50%	75%	97.50%
LI	0.1131	0.1257	0.1327	0.1415	0.1601
Vmax	-2.692	-2.6655	-2.6524	-2.6379	-2.6093
Km	-1.1437	-1.0856	-1.0573	-1.0274	-0.9659

> summary(x3)

Iterations = 1:10000
Thinning interval = 1
Number of chains = 1
Sample size per chain = 10000

1 Empirical mean and standard deviation for each variable, plus standard error of the mean:

	Mean	SD	Naive SE	Time-series SE
LI	0.1344	0.01224	0.0001224	0.0002071
Vmax	-2.6509	0.02058	0.0002058	0.0012024
Km	-1.0544	0.044	0.00044	0.0025179

2 Quantiles for each variable:

	2.50%	25%	50%	75%	97.50%
LI	0.1126	0.1258	0.1335	0.1419	0.1614
Vmax	-2.6904	-2.6651	-2.6505	-2.6376	-2.6089
Km	-1.1393	-1.0839	-1.0539	-1.0256	-0.9653

Female

Female

Log KF L/hr/mg protein Median 95% CI
-7.7880 -9.8580 -5.3120

Male

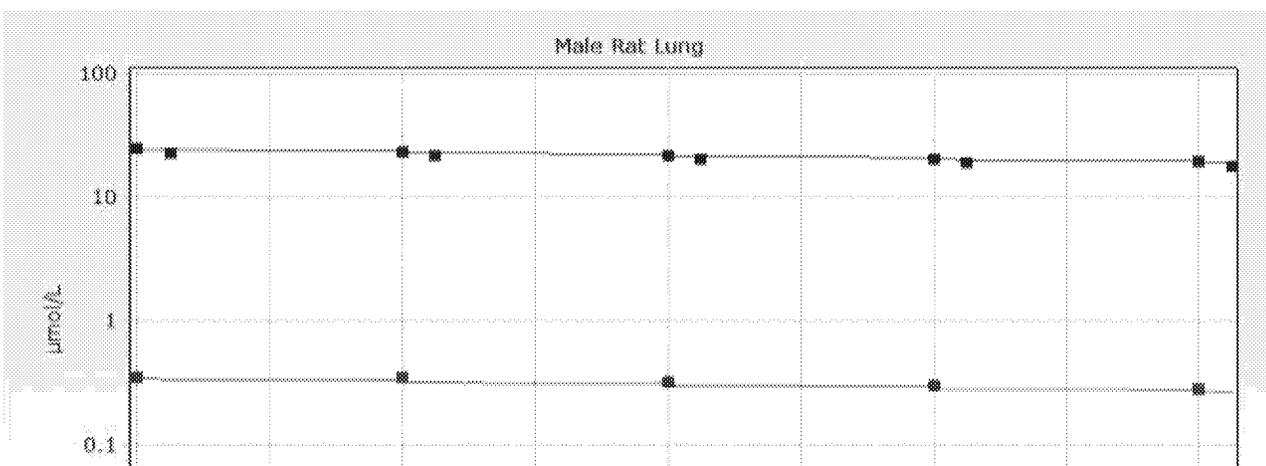
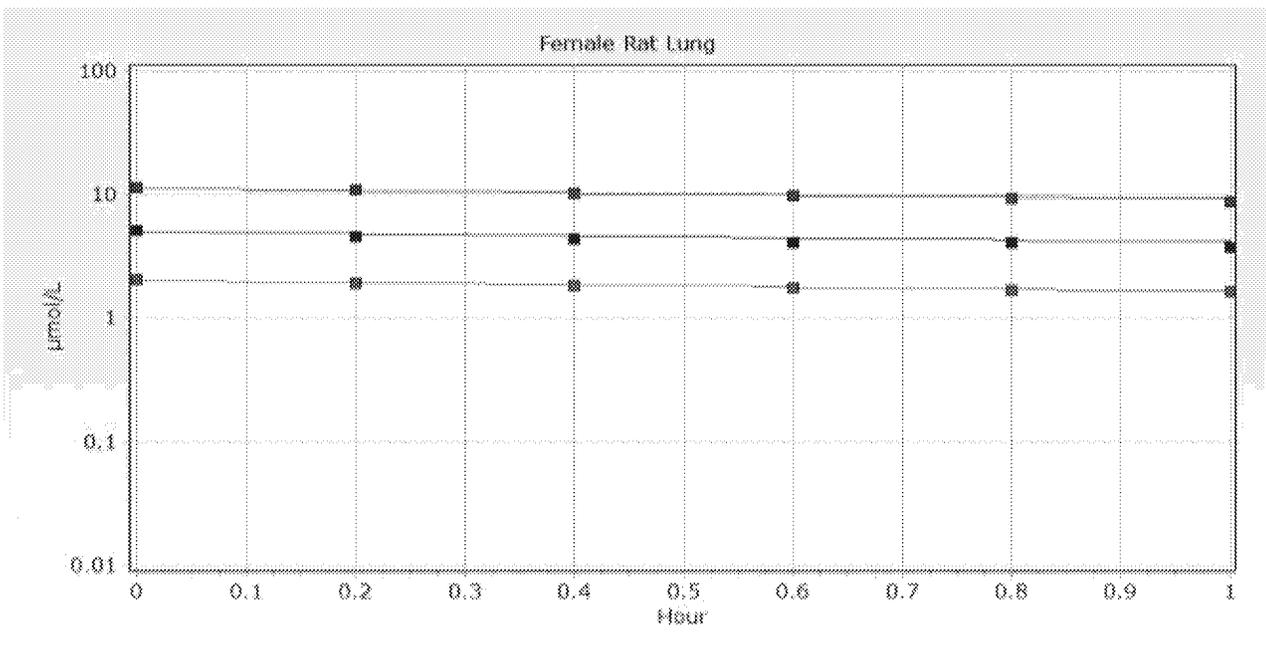
KF L/hr/mg protein Median 95% CI
-7.0480 -9.7970 -4.0630

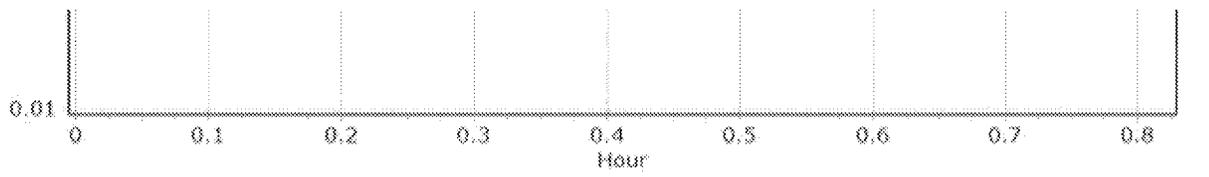
Female

EXP KF L/hr/mg protein Median 95% CI
0.00041 0.000052 0.00493

Male

KF L/hr/mg protein Median 95% CI
0.00087 0.00006 0.0172





gelman.diag(x, autoburnin=FALSE)

male

Potential scale reduction factors:

	Point	est.	Upper	C.I.
LI		1.05	1.16	
KF		1	1	

Multivariate psrf

1.05

>

> summary(x1)

Iterations = 1:10000
 Thinning interval = 1
 Number of chains = 1
 Sample size per chain = 10000

1 Empirical plus mean and standard error of standard deviation for each variable, the mean:

	Mean	SD	Naive	SE	Time-series SE
LI	2.05	0.309	3.09E-03	0.005108	
KF	-7.788	1.284	1.28E-02	0.018051	

2 Quantiles for each variable:

	2.50%	25%	50%	75%	97.50%
LI	1.533	1.828	2.02E+00	2.244	2.721
KF	-9.858	-8.849	-7.82E+00	-6.808	-5.312

> summary(x2)

Iterations = 1:10000
 Thinning interval = 1
 Number of chains = 1
 Sample size per chain = 10000

1 Empirical plus mean and standard error of standard deviation for each variable, the mean:

	Mean	SD	Naive	SE	Time-series SE
LI	2.203	0.3273	3.27E-03	0.005313	
KF	-7.777	1.2763	1.28E-02	0.017886	

2 Quantiles for each variable:

	2.50%	25%	50%	75%	97.50%
LI	1.662	1.968	2.166	2.401	2.945
KF	-9.841	-8.824	-7.828	-6.818	-5.276

> summary(x3)

```

Iterations = 1:10000
Thinning interval = 1.00E+00
Number of chains = 1
Sample size per chain = 10000

```

1 Empirical plus mean and standard deviation for each variable, standard error of the mean:

	Mean	SD	Naive SE	Time-series SE
LI	2.068	0.3201	3.20E-03	0.005258
KF	-7.789	1.2784	1.28E-02	0.018117

2 Quantiles for each variable:

	2.50%	25%	50%	75%	97.50%
LI	1.534	1.841	2.036	2.263	2.774
KF	-9.865	-8.815	-7.842	-6.823	-5.3

gelman.diag(x, autoburnin=FALSE)

Potential scale reduction factors:

	Point	est.	Upper	C.I.
LI		1.05	1.16	
KF		1	1	

Multivariate psrf

1.05

>

> summary(x1)

Iterations = 1:10000
 Thinning interval = 1
 Number of chains = 1
 Sample size per chain = 10000

1 Empirical plus mean and standard error of the mean: standard deviation for each variable, the mean:

	Mean	SD	Naive SE	Time-series SE
LI	2.04	0.3347	0.003347	0.005455
KF	-7.048	1.6157	0.016157	0.021677

2 Quantiles for each variable:

	2.50%	25%	50%	75%	97.50%
LI	1.487	1.803	2.001	2.24	2.815
KF	-9.797	-8.355	-7.058	-5.784	-4.063

> summary(x2)

Iterations = 1:10000
 Thinning interval = 1
 Number of chains = 1
 Sample size per chain = 10000

1 Empirical plus mean and standard error of the mean: standard deviation for each variable, the mean:

	Mean	SD	Naive SE	Time-series SE
LI	2.179	0.3438	0.003438	0.005596
KF	-7.015	1.5991	0.015991	0.021262

2 Quantiles for each variable:

	2.50%	25%	50%	75%	97.50%
LI	1.6	1.942	2.152	2.383	2.938
KF	-9.804	-8.299	-7.006	-5.784	-4.053

> summary(x3)

```

Iterations = 1:10000
Thinning interval = 1
Number of chains = 1
Sample size per chain = 10000

```

1 Empirical plus mean and standard error of the standard deviation for each variable, the mean:

	Mean	SD	Naive SE	Time-series SE
LI	2.019	0.3376	0.003376	0.005777
KF	-7.087	1.599	0.01599	0.021289

2 Quantiles for each variable:

	2.50%	25%	50%	75%	97.50%
LI	1.468	1.777	1.973	2.218	2.813
KF	-9.811	-8.396	-7.077	-5.84	-4.137

Female

Female

			Average	95% CI	
Log	Vmax	$\mu\text{mol/hr/mg protein}$	-5.650	-5.904	-5.39
	Km	$\mu\text{mol/L}$	-0.599	-0.912	-0.28

Male

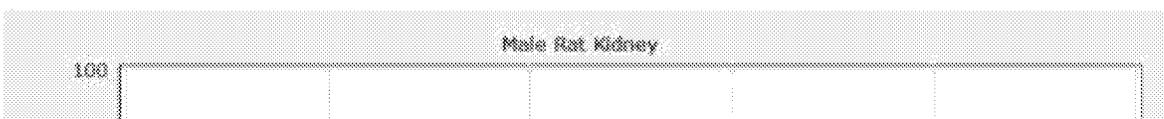
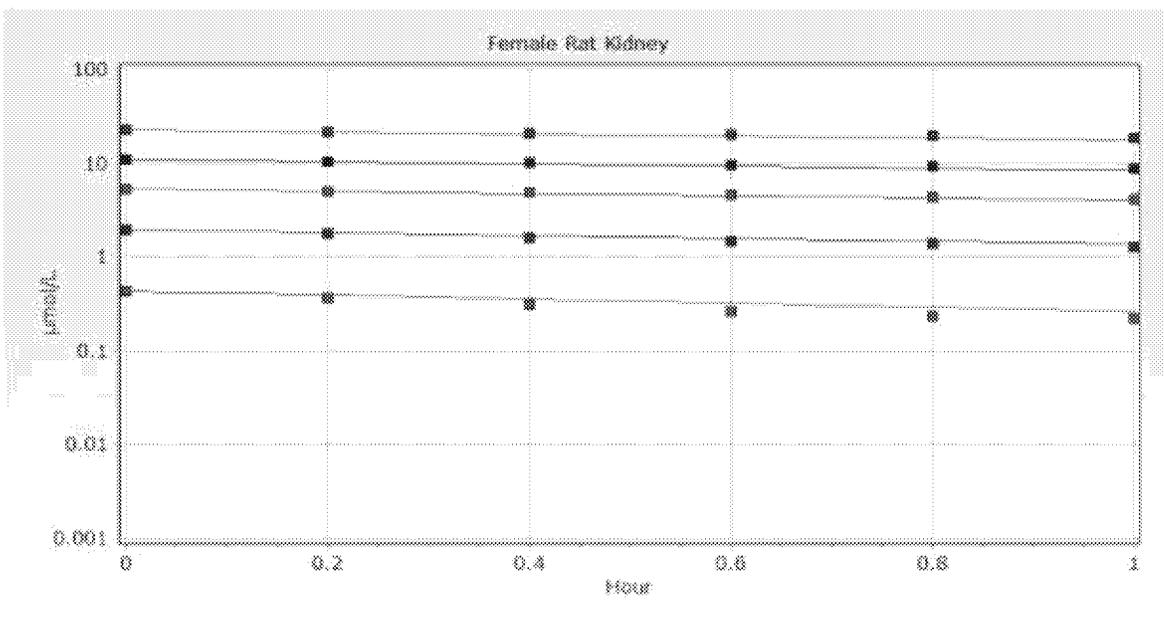
			Average	95% CI	
	Vmax	$\mu\text{mol/hr/mg protein}$	-5.51	-5.77	-5.22
	Km	$\mu\text{mol/L}$	-0.17	-0.49	0.16

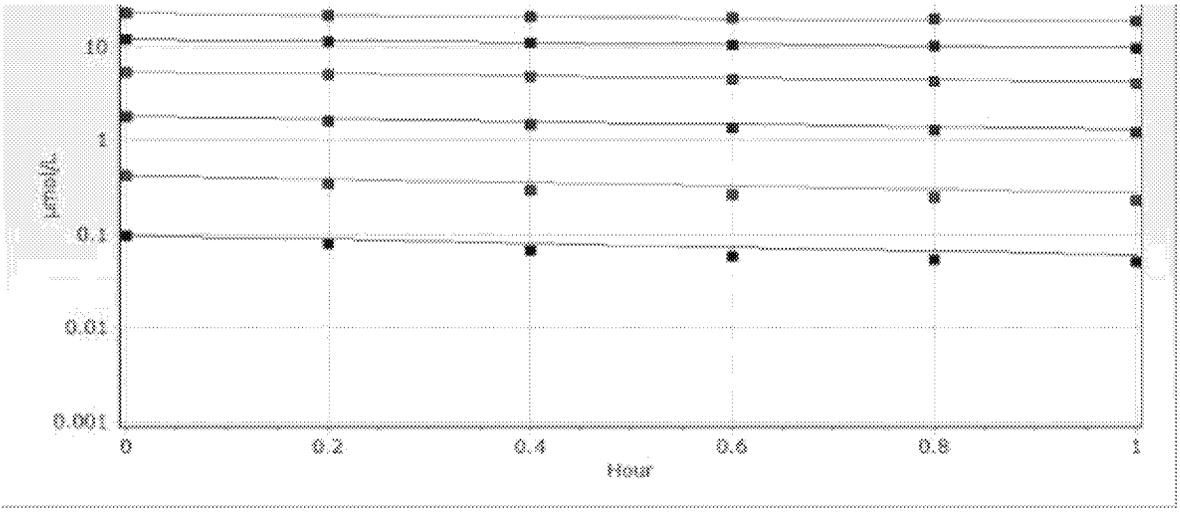
Female

			Average	95% CI	
EXP	Vmax	$\mu\text{mol/hr/mg protein}$	0.0035	0.0027	0.0046
	Km	$\mu\text{mol/L}$	0.55	0.40	0.76

Male

			Average	95% CI	
	Vmax	$\mu\text{mol/hr/mg protein}$	0.0041	0.0031	0.0054
	Km	$\mu\text{mol/L}$	0.84	0.61	1.18





gelman.diag(x, autoburnin=FALSE)

Potential scale reduction factors:

	Point	est.	Upper	C.I.
LI		1	1	
Vmax		1.01	1.01	
Km		1.01	1.01	

Multivariate psrf

1

>

> summary(x1)

Iterations = 1:10000
 Thinning interval = 1
 Number of chains = 1
 Sample size per chain = 10000

1 Empirical plus mean and standard deviation for each variable, standard error of the mean:

	Mean	SD	Naive	SE	Time-series SE
LI	0.05173	0.006683	6.68E-05	1.10E-04	
Vmax	-5.65033	0.130268	1.30E-03	9.59E-03	
Km	-0.59938	0.160524	1.61E-03	1.16E-02	

2 Quantiles for each variable:

	2.50%	25%	50%	75%	97.50%
LI	0.04053	0.04693	0.05125	0.05584	0.06675
Vmax	-5.90355	-5.74056	-5.65076	-5.56237	-5.38774
Km	-0.91238	-0.70759	-0.60173	-0.49152	-0.27719

> summary(x2)

Iterations = 1:10000
 Thinning interval = 1
 Number of chains = 1
 Sample size per chain = 10000

1 Empirical plus mean and standard deviation for each variable, standard error of the mean:

	Mean	SD	Naive	SE	Time-series SE
LI	0.05161	0.006409	6.41E-05	1.03E-04	
Vmax	-5.65309	0.140733	1.41E-03	1.15E-02	

Km -0.60259 0.17301 1.73E-03 1.40E-02

2 Quantiles for each variable:

	2.50%	25%	50%	75%	97.50%
LI	0.04078	0.04703	0.05111	0.05564	0.0655
Vmax	-5.93537	-5.74771	-5.64618	-5.553	-5.3921
Km	-0.95007	-0.72112	-0.59589	-0.47809	-0.2866

> summary(x3)

Iterations = 1:10000
Thinning interval = 1
Number of chains = 1
Sample size per chain = 10000

1 Empirical mean and standard deviation for each variable, plus standard error of the mean:

	Mean	SD	Naive SE	Time-series SE
LI	0.05208	0.00656	6.56E-05	1.12E-04
Vmax	-5.63819	0.15445	1.54E-03	1.35E-02
Km	-0.58345	0.18904	1.89E-03	1.66E-02

2 Quantiles for each variable:

	2.50%	25%	50%	75%	97.50%
LI	0.04121	0.04732	0.0513	0.05622	0.06658
Vmax	-5.94001	-5.73934	-5.6421	-5.53731	-5.31548
Km	-0.96118	-0.70629	-0.5889	-0.46451	-0.19042

Male gelman.diag(x, autoburnin=TRUE)

Potential scale reduction factors:

	Point	est.	Upper	C.I.
LI		1	1.01	
Vmax		1.02	1.07	
Km		1.02	1.07	

Multivariate psrf

1.02

>

> summary(x1)

Iterations = 1:10000
 Thinning interval = 1
 Number of chains = 1
 Sample size per chain = 10000

1 Empirical plus mean and standard deviation for each variable, standard error of the mean:

	Mean	SD	Naive	SE	Time-series SE
LI	0.03728	0.004749	4.75E-05	8.11E-05	
Vmax	-5.50646	0.137464	1.38E-03	1.18E-02	
Km	-0.17303	0.165471	1.66E-03	1.45E-02	

2 Quantiles for each variable:

	2.50%	25%	50%	75%	97.50%
LI	0.02942	0.03383	0.0369	0.04031	0.04757
Vmax	-5.77049	-5.6005	-5.5066	-5.41614	-5.22128
Km	-0.49155	-0.28561	-0.1706	-0.06493	0.16198

> summary(x2)

Iterations = 1:10000
 Thinning interval = 1
 Number of chains = 1
 Sample size per chain = 10000

1 Empirical plus mean and standard deviation for each variable, standard error of the mean:

	Mean	SD	Naive	SE	Time-series SE
LI	0.03707	0.004638	4.64E-05	7.71E-05	
Vmax	-5.51818	0.132386	1.32E-03	1.11E-02	

Km -0.18764 0.159757 1.60E-03 1.32E-02

2 Quantiles for each variable:

	2.50%	25%	50%	75%	97.50%
LI	0.02913	0.03379	0.03667	0.03985	0.04744
Vmax	-5.76623	-5.60823	-5.51901	-5.43725	-5.25247
Km	-0.48377	-0.29546	-0.19014	-0.08872	0.13471

> summary(x3)

Iterations = 1:10000
Thinning interval = 1
Number of chains = 1
Sample size per chain = 10000

1 Empirical mean and standard deviation for each variable, plus standard error of the mean:

	Mean	SD	Naive SE	Time-series SE
LI	0.0371	0.004785	4.79E-05	8.59E-05
Vmax	-5.5344	0.135402	1.35E-03	1.20E-02
Km	-0.2076	0.163251	1.63E-03	1.49E-02

2 Quantiles for each variable:

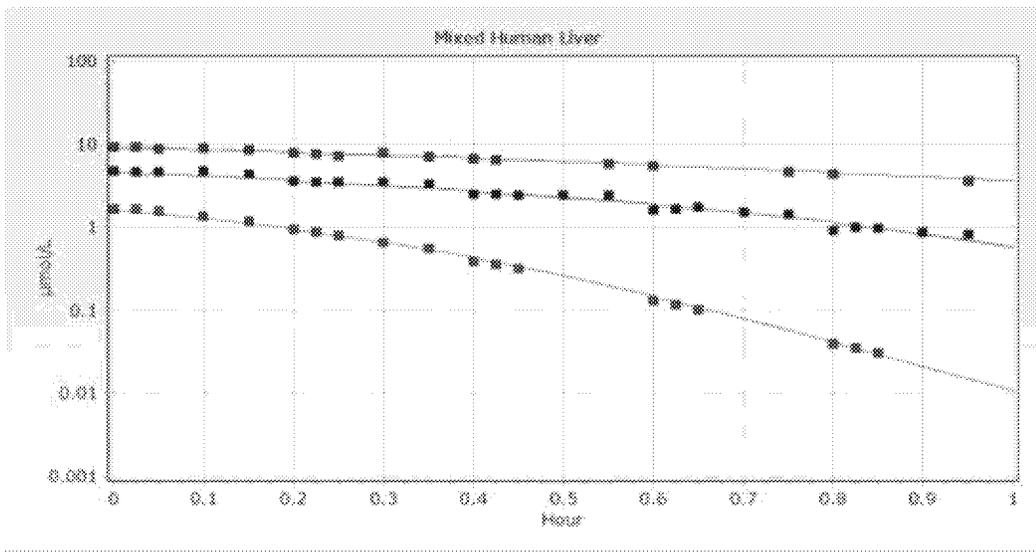
	2.50%	25%	50%	75%	97.50%
LI	0.02927	0.03374	0.03665	0.04004	0.04774
Vmax	-5.81117	-5.62335	-5.53361	-5.44755	-5.26298
Km	-0.5343	-0.31428	-0.20534	-0.1016	0.12265

Mixed Human

			Average	95% CI	
Log	Vmax	$\mu\text{mol/hr/mg protein}$	-2.959	-2.992	-2.93
	Km	$\mu\text{mol/L}$	-1.151	-1.223	-1.08

Mixed Human

			Average	95% CI	
EXP	Vmax	$\mu\text{mol/hr/mg protein}$	0.052	0.050	0.054
	Km	$\mu\text{mol/L}$	0.32	0.29	0.34
		mg/L	0.028		



gelman.diag(x, autoburnin=FALSE)

Potential scale reduction factors:

	Point	est.	Upper	C.I.
LI		1	1	
Vmax		1	1	
Km		1	1	

Multivariate psrf

1

>

>

> summary(x1)

Iterations = 1:10000
 Thinning interval = 1
 Number of chains = 1.00E+00
 Sample size per chain = 1.00E+04

1 Empirical plus mean and standard deviation for each variable, standard error of the mean:

	Mean	SD	Naive	SE	Time-series SE
LI	0.0752	0.007174	7.17E-05	1.19E-04	
Vmax	-2.959	0.016627	1.66E-04	8.95E-04	
Km	-1.1505	0.036055	3.61E-04	0.0019567	

2 Quantiles for each variable:

	2.50%	25%	50%	75%	97.50%
LI	0.06268	0.07012	0.07455	0.07973	0.09091
Vmax	-2.99176	-2.96974	-2.95915	-2.95E+00	-2.93E+00
Km	-1.22304	-1.1739	-1.14973	-1.13E+00	-1.08E+00

> summary(x2)

Iterations = 1:10000
 Thinning interval = 1
 Number of chains = 1
 Sample size per chain = 10000

1 Empirical plus mean and standard deviation for each variable, standard error of the mean:

	Mean	SD	Naive	SE	Time-series SE
LI	0.07538	0.007224	7.22E-05	1.19E-04	

Vmax	-2.95972	0.017136	1.71E-04	9.60E-04
Km	-1.15194	0.037421	3.74E-04	0.0020647

2 Quantiles for each variable:

	2.50%	25%	50%	75%	97.50%
LI	0.06297	0.07038	0.07471	0.07973	0.09108
Vmax	-2.99237	-2.97153	-2.95972	-2.94869	-2.92415
Km	-122.25%	-118%	-115%	-113%	-107.53%

> summary(x3)

Iterations	=	1:10000		
Thinning	interval	=	1	
Number	of	chains	=	1
Sample	size	per	chain	= 10000

1 Empirical plus mean and standard error of standard deviation for each variable, the mean:

	Mean	SD	Naive	SE	Time-series SE
LI	0.07531	0.007241	7.24E-05	1.22E-04	
Vmax	-2.95863	0.016767	1.68E-04	9.04E-04	
Km	-1.1494	0.036705	3.67E-04	0.0020248	

2 Quantiles for each variable:

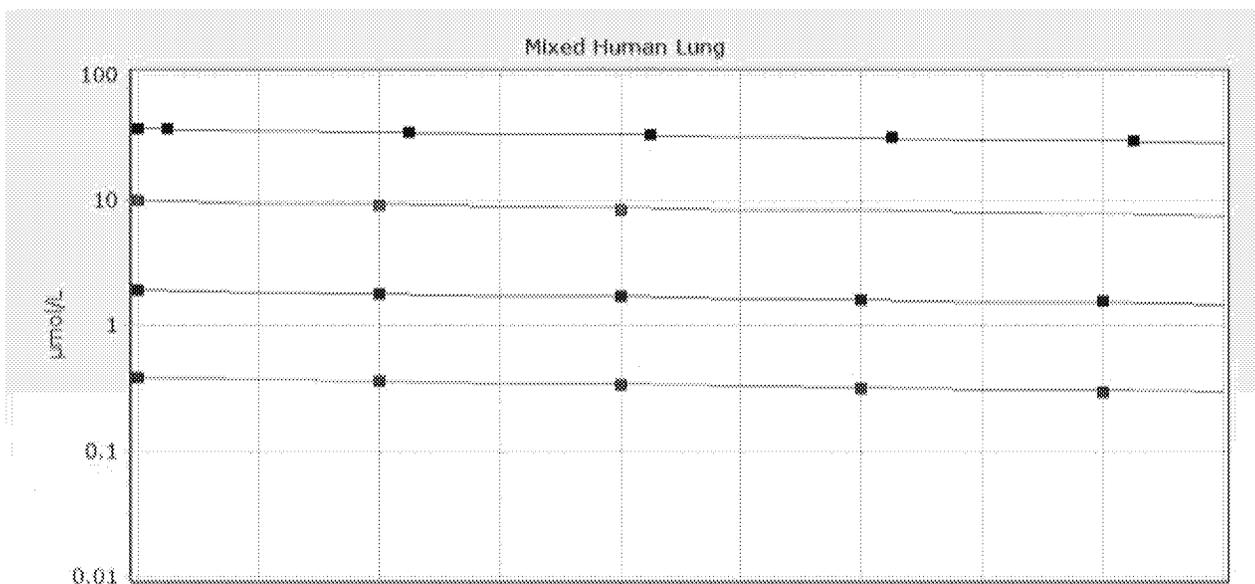
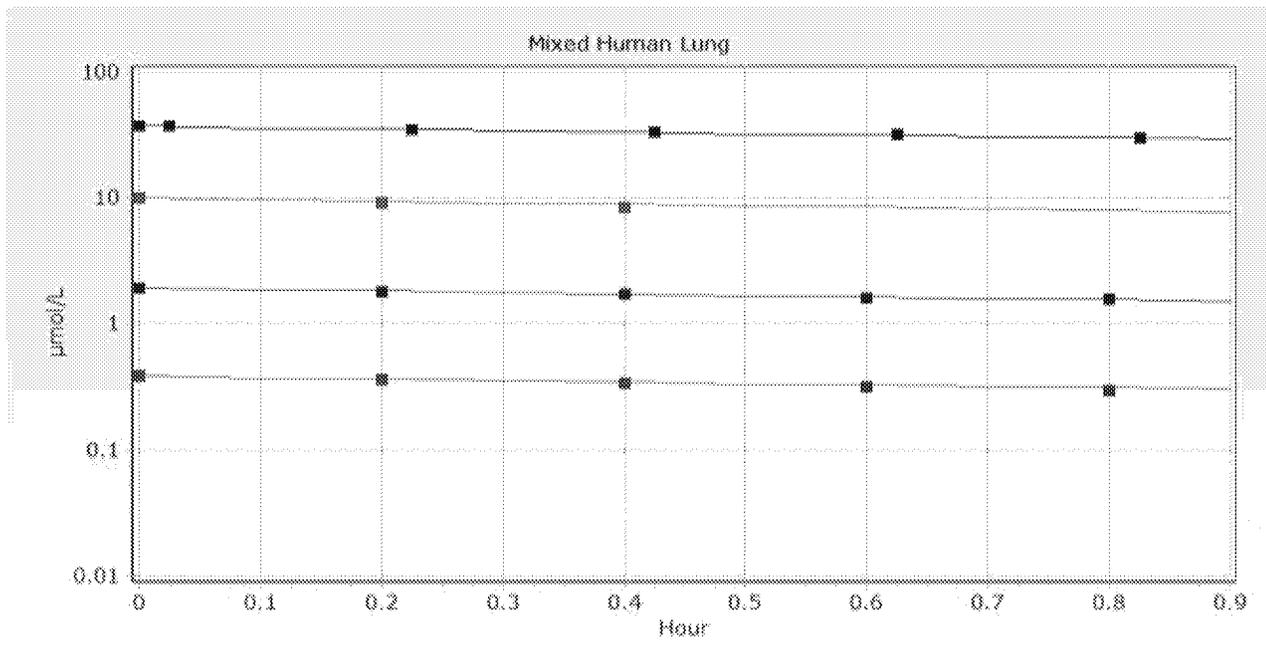
	2.50%	25%	50%	75%	97.50%
LI	0.0629	0.07017	7.46E-02	0.07974	0.09132
Vmax	-2.9931	-2.96951	-2.95856	-2.94749	-2.9265
Km	-1.2237	-1.17323	-1.14921	-1.12577	-1.07885

Mixed Human Lung Microsomes

			Mean	95% CI	
Log	KF	L/hr/mg protein	-31.23	-57.38	-7.84

Mixed

			Mean	95% CI	
EXP	KF	L/hr/mg protein	2.73E-14	1.20E-25	3.92E-04



0 0.1 0.2 0.3 0.4 0.5 0.6 0.7 0.8 0.9
Hour

gelman.diag(x, autoburnin=TRUE)

Potential scale reduction factors:

	Point	est.	Upper	C.I.
LI		1	1	
KF		1	1	

Multivariate psrf

1

>

> summary(x1)

Iterations = 1:10000
Thinning interval = 1.00E+00
Number of chains = 1.00E+00
Sample size per chain = 10000

1 Empirical mean and standard deviation for plus standard error of the mean:

	Mean	SD	Naive	SE	Time-series SE
LI	0.034	1%	6.13E-05	1.08E-04	
KF	-31.23142	14.694963	1.47E-01	3.65E-01	

2 Quantiles for each variable:

	2.50%	25%	50%	75%	97.50%
LI	0.02433	0.02964	0.03306	0.03716	0.0483
KF	-57.37815	-43.13352	-31.0057	-18.57369	-7.8447

> summary(x2)

Iterations = 1:10000
Thinning interval = 1.00E+00
Number of chains = 1
Sample size per chain = 10000

1 Empirical mean and standard deviation for plus standard error of the mean:

	Mean	SD	Naive	SE	Time-series SE
LI	0.0336	0.00595	5.95E-05	1.01E-04	
KF	-31.5983	14.85774	1.49E-01	3.44E-01	

2 Quantiles for each variable:

	2.50%	25%	50%	75%	97.50%
LI	0.0244	0.02933	0.03282	0.03691	0.04755
KF	-57.854	-44.03319	-31.24514	-18.93578	-7.93

> summary(x3)

```

Iterations = 1:10000
Thinning interval = 1
Number of chains = 1
Sample size per chain = 10000

1 Empirical mean and standard deviation for
plus standard error of the mean:

Mean SD Naive SE Time-series SE
LI 0.03377 0.0059 5.90E-05 1.01E-04
KF -31.14584 14.9204 1.49E-01 3.53E-01

```

2 Quantiles for each variable:

	2.50%	25%	50%	75%	97.50%
LI	0.02438	0.02958	0.03305	0.0371	0.0476
KF	-57.58128	-43.38016	-31.06081	-18.1723	-7.8754

each variable,

each variable,

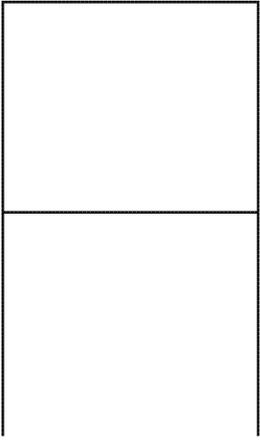
each variable,

MCMC Mean Parameters

		Liver			Mean	Lung		Mean	Kidney		
		Mean	95% CI			95% CI			95% CI		
Kg estimated	Male Mouse	Vmax ($\mu\text{mol/hr/mg protein}$)	0.23	0.22	0.24	0.13	0.12	0.15	0.010	0.008	0.013
		Km ($\mu\text{mol/L}$)	0.61	0.54	0.69	1.72	1.51	2.02	0.58	0.42	0.79
	Female Mouse	Vmax ($\mu\text{mol/hr/mg protein}$)	0.108	0.090	0.13	0.028	0.020	0.039			
		Km ($\mu\text{mol/L}$)	0.46	0.31	0.69	2.91	1.99	4.24			
		KF (L/hr/mg protein)							0.00043	0.00019	0.00071
	Male Rat	Vmax ($\mu\text{mol/hr/mg protein}$)	0.071	0.068	0.074				0.0041	0.0031	0.0054
		Km ($\mu\text{mol/L}$)	0.35	0.32	0.38				0.84	0.61	1.18
		KF (L/hr/mg protein)				0.00087	0.000056	0.0172			
	Female Rat	Vmax ($\mu\text{mol/hr/mg protein}$)	0.072	0.058	0.087				0.0035	0.0027	0.0046
		Km ($\mu\text{mol/L}$)	0.74	0.57	0.96				0.55	0.40	0.76
		KF (L/hr/mg protein)				0.00041	0.000052	0.00493			
	Human	Vmax ($\mu\text{mol/hr/mg protein}$)	0.052	0.050	0.054	7.42E-05			Not Measured		
		Km ($\mu\text{mol/L}$)	0.32	0.29	0.34	3.16E-01					
		KF (L/hr/mg protein)				2.34E-04	1.2E-25	3.9E-04			
						2.73E-14	<- from human lung tab				

Summary In Vivo

**Scaling factors
for average
adults in each
species**



References

Parameters

Revised Scaling

Parameter
B6C3F1 Mouse (Female)
B6C3F1 Mouse (Male)
F344 Rat (Female)
F344 Rat (Male)

Average Human

Reference

1. Brown et al., 1997, *Toxicol. Ind. Health*, July-Aug;13(4):407-84. Review. PubMed PMID:9249
2. Barter et al., *Drug Metab Dispos.* 2008 Dec;36(12):2405-9. doi: 10.1124/dmd.108.021311. E
3. Himmelstein et al., *Toxicol Sci.* 2004b May;79(1):28-37. Epub 2004 Feb 19. PubMed PMID: 1
4. Houston and Galetin, *Curr Drug Metab.* 2008 Nov;9(9):940-51. Review. PubMed PMID: 189
5. Scotcher et al., *Drug Metab Dispos.* 2017 May;45(5):556-568. doi: 10.1124/dmd.117.07524

		Liver	Lung	Kidney
Male Mouse	Vmax (mg/hr/BW ^{0.75})	17.50	0.87	0.074
	Km (mg/L)	0.054	0.15	0.051
Female Mouse	Vmax (mg/hr/BW ^{0.75})	7.95	0.18	
	Km (mg/L)	0.041	0.26	
	KFKIC (L/hr/kg BW)			0.079
Male Rat	Vmax (mg/hr/BW ^{0.75})	7.49		0.024
	Km (mg/L)	0.031		0.074
	KFLUC (L/hr/kg BW)		0.092	
Female Rat	Vmax (mg/hr/BW ^{0.75})	7.04		0.019
	Km (mg/L)	0.066		0.049
	KFLUC (L/hr/kg BW)		0.084	
Human	Vmax (mg/hr/BW ^{0.75})	17.07	0.0033	
	Km (mg/L)	0.028	0.028	

BW (kg)	Liver fractional weight (VLC)	Lung fractional weight (VLUC)	Kidney fractional weight (VKC)	Liver mg microsomal protein per g liver (MPPGL)
0.035	0.0549	0.0073	0.0167	35
0.04	0.0549	0.0073	0.0167	35
0.33	0.0366	0.005	0.0073	40
0.45	0.0366	0.005	0.0073	40

70	0.0257	0.0076	0.0044	50
Brown et al, 1997 (page 415 in text)	Brown et al, 1997 (Tables 4, 5, & 7)	Brown et al, 1997 (Tables 4, 5, & 7)	Brown et al, 1997 (Tables 4, 5, & 7)	Houston and Galetin, 2008 for rat; Barter et al., 2008 for human; rat value used for mouse

929

pub 2008 Sep 5. PubMed PMID: 18775982.

L4976335.

91591.

2. Epub 2017 Mar 7. PubMed PMID: 28270564; PubMed Central PMCID: PMC539964.

Lung mg microsomal protein per g lung (MPPGLU)	Kidney mg microsomal protein per g kidney (MPPGK)	MW
23	11	88.53650
23	11	g/mol = ug/umol
23	11	
23	11	

Biological Scaling	Vmaxc (mg/h/kg BW^{0.75})	In Vitro Value
Female Mouse	Values	0.108
LIVER	Scaling & calculation	
	Unit	umol/h/mg MP

23	11	
Same as Himmelstein et al., 2004b	Based on Scotcher et al., 2017	

Biological Scaling	Vmaxc (mg/h/kg BW^{0.75})	In Vitro Value
Male Mouse	Values	0.230
LIVER	Scaling & calculation	
	Unit	umol/h/mg MP

Biological Scaling	Vmaxc (mg/h/kg BW^{0.75})	In Vitro Value
Female Rat	Values	0.072
LIVER	Scaling & calculation	
	Unit	umol/h/mg MP

Biological Scaling	Vmaxc (mg/h/kg BW^{0.75})	In Vitro Value
Male Rat	Values	0.071
LIVER	Scaling & calculation	
	Unit	umol/h/mg MP

8.

Biological Scaling	Vmaxc (mg/h/kg BW ^{0.75})	In Vitro Value
Mixed gender Human	Values	0.052
LIVER	Scaling & calculation	
	Unit	umol/h/mg MP

x Scaling factor	x Tissue weight	/BW ^{0.75}	x MW = In vivo parameter (unit in PBPK model)
35.00	7.27	89.82	7.95
x MPPGL (mg MP/g liver)	x BW (kg) x VLC x 1000 (g/kg)	/BW ^{0.75}	x MW (ug/umol)/1000 (ug/mg)
umol/h/g liver	umol/h	umol/h/kg BW ^{0.75}	mg/h/kg BW ^{0.75}

Biological Scaling	VmaxLUC (mg/h/kg BW ^{0.75})
Female Mouse	Values
LUNG	Scaling & calculation
	Unit

x Scaling factor	x Tissue weight	/BW^{0.75}	x MW = In vivo parameter (unit in PBPK model)
35.00	17.68	197.64	17.50
x MPPGL (mg MP/g liver)	x BW (kg) x VLC x 1000 (g/kg)	/BW^{0.75}	x MW (ug/umol)/1000 (ug/mg)
umol/h/g liver	umol/h	umol/h/kg BW^{0.75}	mg/h/kg BW^{0.75}

Biological Scaling	VmaxLUC (mg/h/kg BW^{0.75})
Male Mouse	Values
LUNG	Scaling & calculation
	Unit

x Scaling factor	x Tissue weight	/BW^{0.75}	x MW = In vivo parameter (unit in PBPK model)
40.00	34.60	79.47	7.04
x MPPGL (mg MP/g liver)	x BW (kg) x VLC x 1000 (g/kg)	/BW^{0.75}	x MW (ug/umol)/1000 (ug/mg)
umol/h/g liver	umol/h	umol/h/kg BW^{0.75}	mg/h/kg BW^{0.75}

Biological Scaling	KFLUC (L/h/kg BW^{0.75})
Female Rat	Values
LUNG	Scaling & calculation
	Unit

x Scaling factor	x Tissue weight	/BW^{0.75}	x MW = In vivo parameter (unit in PBPK model)
40.00	46.47	84.57	7.49
x MPPGL (mg MP/g liver)	x BW (kg) x VLC x 1000 (g/kg)	/BW^{0.75}	x MW (ug/umol)/1000 (ug/mg)
umol/h/g liver	umol/h	umol/h/kg BW^{0.75}	mg/h/kg BW^{0.75}

Biological Scaling	KFLUC (L/h/kg BW^{0.75})
Male Rat	Values
LUNG	Scaling & calculation
	Unit

x Scaling factor	x Tissue weight	/BW^{0.75}	x MW = In vivo parameter (unit in PBPK model)
50.00	4665.78	192.80	17.07
x MPPGL (mg MP/g liver)	x BW (kg) x VLC x 1000 (g/kg)	/BW^{0.75}	x MW (ug/umol)/1000 (ug/mg)
umol/h/g liver	umol/h	umol/h/kg BW^{0.75}	mg/h/kg BW^{0.75}

Km

0.028019898

Biological Scaling	KFLUC (L/h/kg BW)
Mixed gender Human	Values
LUNG	Scaling & calculation
	Unit

Alternatal Scaling

Biological Scaling	VmaxLUC (mg/h/kg BW^{0.75})
Male Mouse	Values
LUNG	Scaling & calculation
	Unit

In Vitro Value	x Scaling factor	x Tissue weight	/BW ^{0.75}	x MW = In vivo parameter (unit in PBPK model)
0.028	23.00	0.164	2.03	0.18
	x MPPGLU (mg MP/g lung)	x BW (kg) X VLUC X 1000 (g/kg)	/BW ^{0.75}	x MW (ug/umol)/1000 (ug/mg)
umol/h/mg MP	umol/h/g lung	umol/h	umol/h/kg BW ^{0.75}	mg/h/kg BW ^{0.75}

Biological Scaling
Female Mouse
KIDNEY

In Vitro Value	x Scaling factor	x Tissue weight	/BW ^{0.75}	x MW = In vivo parameter (unit in PBPK model)
0.13	23	0.880	9.84	0.87
	x MPPGLU (mg MP/g lung)	x BW (kg) X VLUC X 1000 (g/kg)	/BW ^{0.75}	x MW (ug/umol)/1000 (ug/mg)
umol/h/mg MP	umol/h/g lung	umol/h	umol/h/kg BW ^{0.75}	mg/h/kg BW ^{0.75}

Biological Scaling
Male Mouse
KIDNEY

In Vitro Value	x Scaling factor	x Tissue weight
0.00073	23	0.084
	x MPPGLU (mg MP/g lung)	X VLUC X 1000 (g/kg)
L/h/mg MP	umol/h/g lung	L/h/fraction Lung

Biological Scaling
Female Rat
KIDNEY

In Vitro Value	x Scaling factor	x Tissue weight
0.00080	23	0.092
	x MPPGLU (mg MP/g lung)	X VLUC X 1000 (g/kg)
L/h/mg MP	umol/h/g lung	L/h/fraction Lung

Biological Scaling
Male Rat
KIDNEY

In Vitro Value	x Scaling factor	x Tissue weight
2.34E-04	23	4.10E-02
	x MPPGLU (mg MP/g lung)	X VLUC X 1000 (g/kg)
L/h/mg MP	L/h/g lung	L/h/fraction Lung

Biological Scaling
Mixed gender Human
Kidney

In Vitro Value	x Scaling factor	x Tissue weight	/BW^{0.75}	x MW = In vivo parameter (unit in PBPK model)
7.42E-05	2.30E+01	9.08E-01	3.75E-02	3.32E-03
	x MPPGLU (mg MP/g lung)	x BW (kg) X VLUC X 1000 (g/kg)	/BW^{0.75}	x MW (ug/umol)/1000 (ug/mg)
umol/h/mg MP	umol/h/g lung	umol/h	umol/h/kg BW^{0.75}	mg/h/kg BW^{0.75}

KFKIC (L/h/kg BW^{0.75})	In Vitro Value	x Scaling factor	x Tissue weight
Values	0.0004310	11.0	0.07917
Scaling & calculation		x MPPGK (mg MP/g kidney)	x BW (kg) x VKC x 1000 (g/kg)
Unit	L/h/mg MP	L/hr/g kidney	L/hr/fractio n kidney

VmaxKIDc (mg/h/kg BW ^{0.75})	In vitro value (Yang et al. 2012, Table 3)	x Scaling factor	x Tissue weight	/BW ^{0.75}	x MW = In vivo parameter (unit in PBPK model)
Values	0.010	11.0	0.074	0.83	0.0736
Scaling & calculation		x MPPGK (mg MP/g kidney)	x BW (kg) x VKC x 1000 (g/kg)	/BW ^{0.75}	x MW (ug/umol)/10 00 (ug/mg)
Unit	umol/h/mg MP	umol/h/g kidney	umol/h	umol/h/kg BW ^{0.75}	mg/h/kg BW ^{0.75}

VmaxKIDc (mg/h/kg BW ^{0.75})	In Vitro Value	x Scaling factor	x Tissue weight	/BW ^{0.75}	x MW = In vivo parameter (unit in PBPK model)
Values	0.00352	11.0	0.093	0.21	0.019
Scaling & calculation		x MPPGK (mg MP/g kidney)	x BW (kg) x VKC x 1000 (g/kg)	/BW ^{0.75}	x MW (ug/umol)/10 00 (ug/mg)
Unit	umol/h/mg MP	umol/h/g kidney	umol/h	umol/h/kg BW ^{0.75}	mg/h/kg BW ^{0.75}

VmaxKIDc (mg/h/kg BW ^{0.75})	In Vitro Value	x Scaling factor	x Tissue weight	/BW ^{0.75}	x MW = In vivo parameter (unit in PBPK model)
Values	0.00406	11.0	0.147	0.27	0.024
Scaling & calculation		x MPPGK (mg MP/g kidney)	x BW (kg) x VKC x 1000 (g/kg)	/BW ^{0.75}	x MW (ug/umol)/10 00 (ug/mg)
Unit	umol/h/mg MP	umol/h/g kidney	umol/h	umol/h/kg BW ^{0.75}	mg/h/kg BW ^{0.75}

in vitro metabolic constant not reported in Yang et al. 2012

Cell: G22

Comment: [Threaded comment]

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Comment:

35 is value fro Medinsky et al. (1994), stated in Supp Mat C, doesn't match "reference" in row 27 below

Cell: G24

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Comment:

Text on p. 9 says 45

Cell: G26

Comment: [Threaded comment]

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Comment:

Text on p. 9 says 45

Cell: H26

Comment: [Threaded comment]

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Comment:

Text on p. 9 says 20; 23 matches Himmelstein

Uses IVIVE scaling approach from the Yoon report. (human lung Vmax calculated using approach from methylene chlorid

e - scaling liver in vitro v_{max} to lung based on ratio of ethoxycoumarin metabolism in lung to liver)

Dose metrics using parameters derived with MCMC estimate

TSTOP 336 hrs

Exposure: 6 hr/day 5 days/week

Revised parameters from MCMC of In Vitro data with flux limitation included

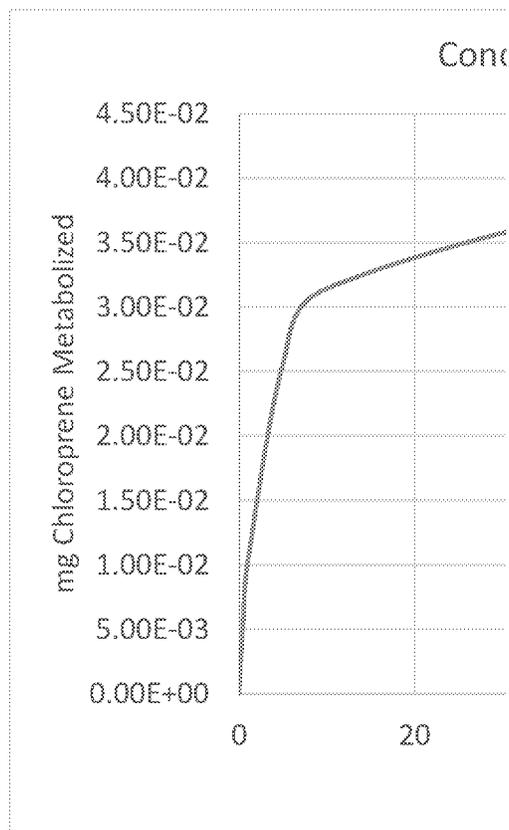
Female Mouse Initial Parm				
ppm	Amt. Metab. Liver	Amt. Metab. Lung	Amt. Metab. Kidney	
12.8	1.22	1.20	0.041	
32	3.12	1.91	0.105	
80	7.93	2.52	0.27	

Human Initial Parm				
ppm	Amt. Metab. Liver	Amt. Metab. Lung	Amt. Metab. Kidney	
12.8	0.30	0.0082	-	
32	0.74	0.012	-	
80	1.85	0.017	-	

Human Continuous Exposure

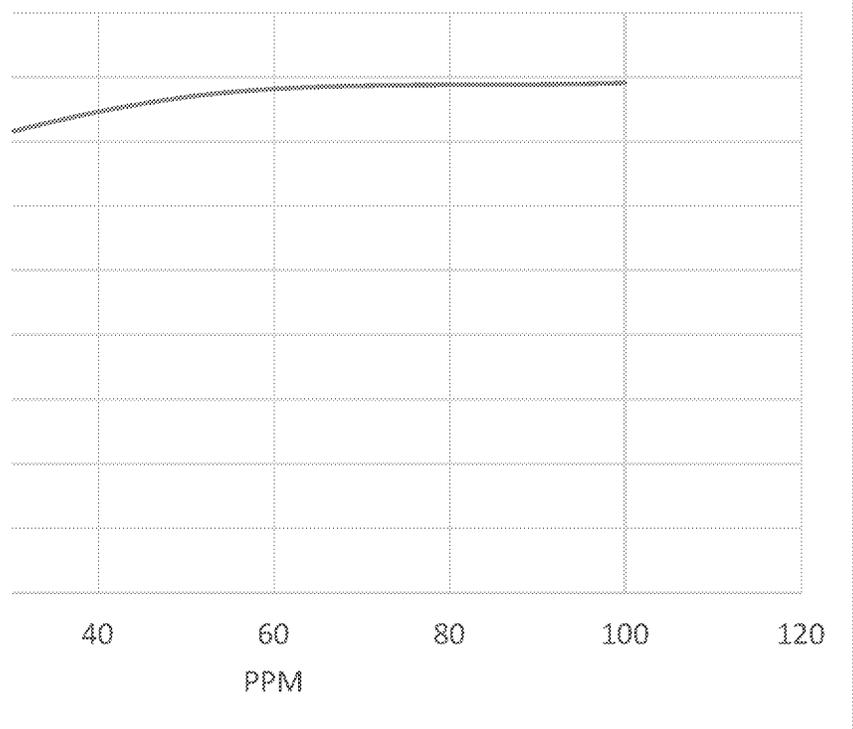
Human Parm Continuous Exposure

PPM	Amt. Metab. Liver	Amt. Metab. Lung	Amt. Metab. Kidney	
2.76E-04	3.51E-05	3.76E-06	-	
1.00E-03	1.27E-04	1.36E-05	-	
5.00E-03	6.35E-04	6.79E-05	-	
1.00E-02	1.27E-03	1.36E-04	-	
5.00E-02	6.36E-03	6.69E-04	-	
1.00E-01	1.27E-02	1.32E-03	-	
5.00E-01	6.37E-02	5.84E-03	-	
1.00E+00	1.28E-01	1.02E-02	-	
5.00E+00	6.42E-01	2.56E-02	-	
1.00E+01	1.29E+00	3.14E-02	-	
5.00E+01	6.45E+00	3.84E-02	-	
1.00E+02	1.29E+01	3.95E-02	-	



of Kgl: 0.22 L/hr

centration Response Lung



Estimates with 0.45 l/hr Kg

Cumulative (mg)
 TSTOP 336 hrs
 Exposure: 6 hr/day 5 days/week

Revised parameters from MCMC of In Vitro data with flux included

Female Mouse Initial Parm			
ppm	Amt. Metab. Liver	Amt. Metab. Lung	Amt. Metab. Kidney
12.8	1.22	1.20	0.040
32	3.11	1.91	0.10
80	7.90	2.52	0.26

Cumulative (mg)

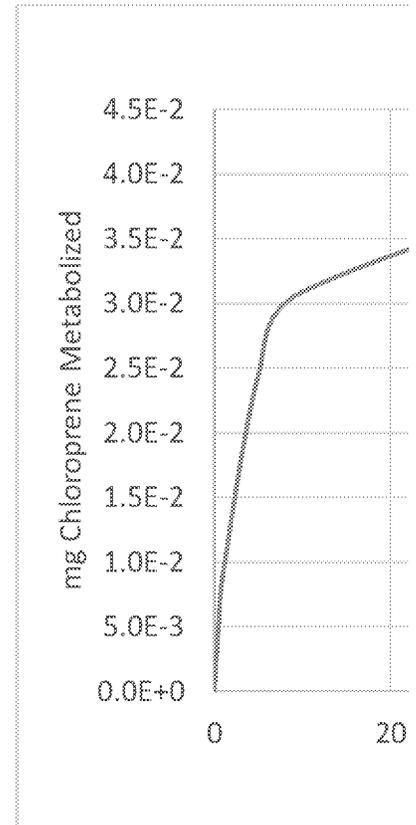
Human Initial Parm			
ppm	Amt. Metab. Liver	Amt. Metab. Lung	Amt. Metab. Kidney
12.8	0.30	0.0078	-
32	0.74	0.0112	-
80	1.85	0.016	-

Cumulative (mg)

Human Continuous Exposure

Human Parm Continuous Exposure

PPM	Amt. Metab. Liver	Amt. Metab. Lung	Amt. Metab. Kidney
2.80E-04	3.56E-05	3.24E-06	-
1.00E-03	1.27E-04	1.16E-05	-
5.00E-03	6.37E-04	5.78E-05	-
1.00E-02	1.27E-03	1.15E-04	-
5.00E-02	6.37E-03	5.71E-04	-
1.00E-01	1.27E-02	1.13E-03	-
5.00E-01	6.38E-02	5.09E-03	-
1.00E+00	1.28E-01	9.09E-03	-
5.00E+00	6.42E-01	2.44E-02	-
1.00E+01	1.29E+00	3.09E-02	-
5.00E+01	6.45E+00	3.91E-02	-
1.00E+02	1.29E+01	4.05E-02	-



Concentration Response Lung

